CLAIMS

What is claimed is:

1. A method for determining whether a subject is predisposed to having an adverse pregnancy outcome, said method comprising the steps of:

a) obtaining a nucleic acid sample from the subject; and

b) detecting an IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2 or an allele in linkage disequilibrium with an IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2 in a sample, wherein detection of the IL-1A (+4845) allele 2 or the IL-1 (-511) allele 2 or the allele in linkage disequilibrium with the IL-1A (+4845) allele 2 or the IL-1 (-511) allele 2 indicates that the fetus is predisposed to an adverse pregnancy outcome.

2. The method of claim 1, wherein the adverse pregnancy outcome is low birth weight.

3. The method of claim 1, wherein said detecting step is selected from the group consisting of allele specific oligonucleotide hybridization; size analysis; sequencing; hybridization; 5' nuclease digestion; single-stranded conformation polymorphism; allele specific hybridization; primer specific extension; and oligonucleotide ligation assay.

4. The method of claim 1, wherein prior to the detection step, the nucleic acid sample is subject to an amplification step.

5. The method of claim 4, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID No: 1 through SEQ ID No:18.

6. The method of claim 3, wherein said size analysis is preceded by a restriction enzyme digestion.

7. A method of claim 6, wherein said restriction enzyme digestion uses a restriction enzyme selected from the group consisting of: *Nco* I, *Alu* I and *Msp* I.

8. A method of identifying an allele associated with an low birth weight, said method comprising identifying an allele, which is in linkage disequilibrium with IL-1A (+4845) allele 2 and/or an IL-1 (-511) allele 2.

9. A kit for determining a subject's susceptibility to delivering a low birth weight baby, said kit comprising a first primer oligonucleotide that hybridizes 5′ or 3' to an IL-1A (+4845) allele 2 and/or an IL-1 (-511) allele 2 or an allele that is in linkage disequilibrium with an IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2.

10. The kit of claim 9, which additionally comprises a second primer oligonucleotide that hybridizes 3' to an IL-1A (+4845) allele 2 or an allele that is in linkage disequilibrium with an IL-1A (+4845) allele 2 when the first primer hybridizes 5' to an IL-1A (+4845) allele 2 or an allele that is in linkage disequilibrium with IL-1A (+4845) allele 2 when the first primer hybridizes 3'.

11. The kit of claim 10, wherein said first primer and said second primer hybridize to a region in the range of between about 50 and 1000 base pairs.

12. The kit of claim 9, 10 or 11, wherein said primer or primers is selected from the group consisting of SEQ ID Nos: 1 through 18.

13. The kit of claim 9, which additionally comprises a detection means.

14. The kit of claim 13, wherein the detection means is selected from the group consisting of: a restriction enzyme, a fluorescent label, a radioactive label, nucleotides, a DNA polymerase and a thermostable DNA polymerase.

15. The kit of claim 9, which additionally comprises an amplification means.

16. The kit of claim 9, which further comprises a control.

17. A method for selecting an appropriate therapeutic to administer to a pregnant woman predisposed to having a low birth weight baby, comprising the steps of: determining the IL-1 or TNF-A genotype of the individual to identify whether the subject contains an low birth weight (LBW) associated allele and selecting a therapeutic that compensates for an LBW causative functional mutation that is in linkage disequilibrium with the polymorphism.

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18. The method of claim 17, wherein the low birth weight baby is pre-term or pre-mature.

19. The method of claim 17, wherein said genotyping is selected from the group consisting of: allele specific oligonucleotide hybridization; size analysis; sequencing; hybridization; 5' nuclease digestion; single-stranded conformation polymorphism; allele specific hybridization; primer specific extension; and oligonucleotide ligation assay.

20. The method of claim 17, wherein prior to the genotyping, the nucleic acid sample is subjected to an amplification step.

21. The method of claim 20, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID No:1 through SEQ ID No:18.

22. The method of claim 19, wherein said size analysis is preceded by a restriction enzyme digestion.

23. The method of claim 22, wherein said restriction enzyme digestion uses a restriction enzyme selected from the group consisting of: *Nco* I, *Alu* I and *Msp* I.

24. The method of claim 17, wherein the therapeutic is selected from the group consisting of: a corticosteroid, antimetabolite, cytotoxic drug, colchicine or an anticytokine.

25. The method of claim 17, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 or TNFα activity.

26. The method of claim 25, wherein the IL-1 is IL-1α.

27. The method of claim 25, wherein the IL-1 is IL-1β.

28. The method of claim 25, wherein the IL-1 is IL-1Ra.

29. The method of claim 25, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

30. The method of claim 25, wherein the modulator is an agonist.

31. The method of claim 25, wherein the modulator is an antagonist.

32. The method of claim 17, wherein the LBW associated allele is IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2 or an allele that is in linkage disequilibrium with IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2.

33. A method for determining the effectiveness of treating an LBW subject with a particular dose of a particular therapeutic, comprising the steps of:

(a) detecting the level, amount or activity of an IL-1 or TNF-α protein; or an IL-1 or TNF-A mRNA or DNA in a sample obtained from a subject or a fetus;
(b) administering the particular dose of the particular therapeutic to the subject; detecting the level, amount or activity of an IL-1 or TNF-α protein; or an IL-1 or TNF-A mRNA or DNA in a sample obtained from a subject; and
(c) comparing the relative level, amount or activity obtained in step (a) with the level, amount or activity obtained in step (b).

34 The method of claim 33, wherein the therapeutic is selected from the group consisting of: a corticosteroid, antimetabolite, cytotoxic drug, colchicine or an anticytokine.

35. The method of claim 33, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 or TNFα activity.

36. The method of claim 35, wherein the IL-1 is IL-1α.

37. The method of claim 35, wherein the IL-1 is IL-1β.

38. The method of claim 35, wherein the IL-1 is IL-1Ra.

39. The method of claim 35, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

40. The method of claim 35, wherein the modulator is an agonist.

41. The method of claim 35, wherein the modulator is an antagonist.

42. A method for treating a subject predisposed to having a low birth weight baby (LBW) comprising the steps of: determining the IL-1 or TNF-A genotype of the individual to identify the presence of an LBW associated allele; and administering to the subject a therapeutic that compensates for an LBW causative mutation that is in linkage disequilibrium with the polymorphism.

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43. The method of claim 42, wherein the low birth weight baby is pre-term or premature.

44. The method of claim 42, wherein said genotyping is selected from the group consisting of: allele specific oligonucleotide hybridization; size analysis; sequencing; hybridization; 5' nuclease digestion; single-stranded conformation polymorphism; allele specific hybridization; primer specific extension; and oligonucleotide ligation assay.

45. The method of claim 42, wherein prior to the genotyping, the nucleic acid sample is subjected to an amplification step.

46. The method of claim 45, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID No:1 through SEQ ID No:18.

47. The method of claim 44, wherein said size analysis is preceded by a restriction enzyme digestion.

48. The method of claim 47, wherein said restriction enzyme digestion uses a restriction enzyme selected from the group consisting of: *Nco* I, *Alu* I and *Msp* I.

49. The method of claim 42, wherein the therapeutic is selected from the group consisting of: a corticosteroid, antimetabolite, cytotoxic drug, colchicine or an anticytokine.

50. The method of claim 42, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 or TNFα activity.

51. The method of claim 50, wherein the IL-1 is IL-1α.

52. The method of claim 50, wherein the IL-1 is IL-1β.

53. The method of claim 50, wherein the IL-1 is IL-1Ra.

54. The method of claim 50, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

55. The method of claim 50, wherein the modulator is an agonist.

56. The method of claim 50, wherein the modulator is an antagonist.

57. The method of claim 42, wherein the LBW associated allele is IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2 or an allele that is in linkage disequilibrium with IL-1A (+4845) allele 2 or an IL-1 (-511) allele 2.

58. A method for screening for an LBW therapeutic comprising the steps of:
a) combining an IL-1 or TNF-α polypeptide or bioactive fragment thereof, an IL-1 or TNF-α binding partner and a test compound under conditions wherein, but for the test compound, the IL-1 or TNF-α protein and IL-1 or TNF-α binding partner are able to interact; and
b) detecting the extent to which, in the presence of the test compound, an IL-1 or TNF-α protein/IL-1 or TNF-α binding partner complex is formed, wherein an increase in the amount of complex formed by an agonist in the presence of the compound relative to in the absence of the compound or a decrease in the amount of complex formed by an antagonist

in the presence of the compound relative to in the absence of the compound indicates that the compound is an LBW therapeutic.

59. The method of claim 58, wherein the agonist or antagonist is selected from the group consisting of: a protein, peptide, peptidomimetic, small molecule or nucleic acid.

60. The method of claim 59, wherein the nucleic acid is selected from the group consisting of: an antisense, ribozyme and triplex nucleic acid.

61. The method of claim 58, which additionally comprises the step of preparing a pharmaceutical composition from the compound.

62. The method of claim 58, wherein the IL-1 is IL-1α.

63. The method of claim 58, wherein the IL-1 is IL-1β.

64. The method of claim 58, wherein the IL-1 is IL-1Ra.

65. A method for identifying a LBW therapeutic, comprising the steps of:
(a) contacting an appropriate amount of the candidate compound with a cell or cellular extract, which expresses an IL-1 or TNF-A gene; and
(b) determining the resulting protein bioactivity, wherein a decrease of an agonist bioactivity or a decrease in an antagonist bioactivity in the presence of the compound as compared to the bioactivity in the absence of the compound indicates that the candidate is an LBW therapeutic.

66. The method of claim 65, wherein the modulator is an antagonist of an IL-1α, IL-1β, or TNFα bioactivity.

67. The method of claim 65, wherein the modulator is an agonist of an IL-1Ra bioactivity.

68. The method of claim 65, wherein in step (b), the protein bioactivity is determined by determining the expression level of the IL-1 or TNF-A gene.

69. The method of claim 65, wherein the expression level is determined by detecting the amount of mRNA transcribed from the IL-1 or TNF-A gene.

70. The method of claim 65, wherein the expression level is determined by detecting the amount of the IL-1 or TNF-A gene product produced.

71. The method of claim 65, wherein the expression level is determined using an anti-the IL-1 or TNF-A antibody in an immunodetection assay.

72. The method of claim 65, which additionally comprises the step of preparing a pharmaceutical composition from the compound.

73. The method of claim 65, wherein said cell is contained in an animal.

74. The method of claim 73, wherein the animal is transgenic.

75. A kit for the prediction of an adverse pregnancy outcome, said kit comprising at least one 5' oligonucleotide that hybridizes 5' to an IL-1 marker and at least one 3' oligonucleotide that hybridizes 3' to said IL-1 marker.

76. The kit of claim 75, wherein said 5' oligonucleotide and said 3' oligonucleotide are between 50 and 1000 base pairs apart when hybridized to an IL-1 gene.

77. The kit of claim 75, further comprising a control sample and a reagent for PCR amplification.

78. The kit of claim 77, further comprising an allele detection means.

79. The kit of claim 78, further comprising a DNA sampling means and a DNA sampling reagent.

80. A method of determining increased susceptibility to an adverse pregnancy outcome, said method comprising:
(a) detecting an IL-1 allele 2 of a marker in a nucleic acid from a specimen collected from a fetus;
wherein detecting said IL-1 allele 2 marker indicates the individual's increased susceptibility to an adverse pregnancy outcome.

81. The method of claim 80, wherein said adverse pregnancy outcome is a premature preterm-low birth weight delivery.

82. The method of claim 80, wherein said detecting comprises PCR amplification of the DNA using a primer that overlaps with an oligonucleotide selected from the group consisting of: SEQ. ID. Nos: 1-18.

83. A method of predicting increased susceptibility to adverse pregnancy outcome comprising: determining a genetic polymorphism pattern in genomic DNA for IL-1A and IL-1B and comparing the pattern to a control sample, wherein the control sample comprises an IL-1A allele 2 and IL-1B (Taq I) allele 2; and wherein the similarity of the genetic polymorphism pattern to the control sample indicates susceptibilty to an adverse pregnancy outcome.

84. The method of claim 83, wherein said step for determining a genetic polymorphism pattern comprises amplification with a PCR primer selected from the group consisting of:

5' TGT TCT ACC ACC TGA ACT AGG C 3' (SEQ ID No: 1);

5' TTA CAT ATG AGC CTT CCA TG 3' (SEQ ID No: 2);

5' TGG CAT TGA TCT GGT TCA TC 3' (SEQ ID No: 3);

5' GTT TAG GAA TCT TCC CAC TT 3' (SEQ ID No: 4);

5' CTC AGG TGT CCT CGA AGA AAT CAA A 3' (SEQ ID No: 5);

5' GCT TTT TTG CTG TGA GTC CCG 3' (SEQ ID No: 6).

5' ATGGTTTTAGAAATCATCAAGCCTAGGGCA 3' (SEQ ID No: 7)

5' AATGAAAGGAGGGGAGGATGACAGAAATGT 3' (SEQ ID No: 8)

5' CTATCTGAGGAACAACCAACTAGTAGC 3' (SEQ ID No: 9)

5' TAGGACATTGCACCTAGGGTTTGT 3' (SEQ ID No: 10)

5' AGGCAATAGGTTTTGAGGGCCAT 3' (SEQ ID No: 11)

5' TCCTCCCTGCTCCGATTCCG 3' (SEQ ID No: 12)

5' GAAGCCCCTCCCAGTTCTAGTTC 3' (SEQ ID No: 13)

5' CACTCCCCATCCTCCCTGGTC 3' (SEQ ID No: 14)

5' CTCAGCAACACTCCTAT 3' (SEQ ID No: 15)

5' TCCTGGTCTGCAGGTAA 3' (SEQ ID No: 16)

5' AAGCTTGTTCTACCACCTGAACTAGGC 3' (SEQ ID No: 17)

5' TTACATATGAGCCTTCCATG 3' (SEQ ID No: 18)